UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,258	07/21/2005	Min-Ho Shong	20050-00003	2722

7590 04/04/2008

JHK Law
P.O. Box 1078
La Canada, CA 91012-1078

EXAMINER	
WORLEY, CATHY KINGDON	
ART UNIT	PAPER NUMBER
1638	

MAIL DATE	DELIVERY MODE
04/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,258	SHONG ET AL.	
	Examiner	Art Unit	
	CATHY K. WORLEY	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-14* is/are pending in the application.

4a) Of the above claim(s) *6 and 11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed Jan. 30, 2008, has been entered.

2. Claim 5 has been cancelled.

Claims 1-4 and 6-14 are pending.

Claims 6 and 11-14 are withdrawn.

3. Claims 1-4 and 7-10 are examined in the present office action.

4. This application contains recitations in claims 1 and 7 drawn to an invention nonelected with traverse in the response filed May 8, 2007. This application also contains claims 6 and 11-14 which were nonelected with traverse in the response filed May 8, 2007. A complete reply to the final rejection must include cancellation of nonelected claims and subject matter or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

5. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

Objections that are withdrawn

6. The objections to the specification for hyperlinks and a trademark are withdrawn in light of the Applicant's amendments to the specification.

7. The warning for potential objection to claim 7 for being a duplicate of claim 5 is withdrawn in light of the Applicant's cancellation of claim 5.

Claim Rejections - 35 USC § 103

8. Claims 1-4 and 7-10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Whitelam (J. Sci. Food Agric. (1995) Vol. 68, pp. 1-9) in view of each of Stiens et al (Biotechnol. Prog. (2000) Vol. 16, pp. 703-709), Mullins et al (J. Clin. Invest. (1995) Vol. 96, pp. 30-37), and Takeo et al (EP 0 719 858 A2 (1996)) for the reasons of record stated in the previous Office Action mailed on July 30, 2007. The Applicant's arguments in the response filed on Jan. 30, 2008, were fully considered but were not found to be persuasive.

The claims are drawn to a method of producing human thyroid stimulating hormone receptor (hTSHR)

Whitelam teaches the production of recombinant proteins in plants, including the use of an *Agrobacterium tumefaciens* binary vector system to transform tobacco plants, which are *Nicotiana tabacum* (see page 3, left column). Whitelam teaches the use of the CaMV 35S promoter which functions in plants (see page 3, left column). Whitelam teaches purification of a recombinant protein from a transgenic plant (see page 2, right column). Whitelam teaches that mRNA from a transgene was produced in the plant (see third paragraph on page 6) which indicates that the construct comprised a functional polyadenylation signal. Whitelam teaches the selection of a stable transgenic line (see second paragraph on page 4), and the steps of selecting transformed plant cells and regenerating a plant from said cells in order to generate a stable transgenic line are necessary steps that are well-known in the

art and are required in order to generate a stable transgenic plant, therefore they are in intrinsic part of the method taught by Whitelam.

Whitelam does not teach recombinant hTSHR.

Stiens et al teach recombinant hTSHR produced in human leukemia cells (see last paragraph on page 704). Mullins et al teach recombinant hTSHR produced in B-cells (see right column on page 31). Takeo et al teach recombinant hTHSR produced in a myeloma cell line (see abstract).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to utilize the methods taught by Whitelam to produce the hTSHR taught by Stiens et al, Mullins et al or Takeo et al. One would have been motivated to do so because Takeo et al, Stiens et al, and Mullins et al teach that recombinant hTSHR has commercial value for use in diagnostic tests (see Takeo, column 1, lines 43-51; and Stiens, second paragraph, left column, page 703; and Mullins, first paragraph, page 30). Given the successes of Stiens et al, Mullins et al, and Takeo et al in producing recombinant hTSHR and given the successes of producing other recombinant therapeutic proteins in transgenic plants taught by Whitelam, one of ordinary skill in the art would expect to succeed in expressing hTSHR in transgenic plants.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (In re Opprecht 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); In re Bode 193 USPQ 12

(CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The Applicant argues that one of skill in the art would not have had a reasonable expectation of success in combining these references because hTSHR is an animal protein and attempts to express it in bacteria, yeast, and insect cells were not successful (see paragraph bridging pages 7-8 of the response), and that difficulties surrounding expression of animal protein in non-mammalian cells have been reported and documented (see third paragraph on page 8 of the response).

This is not persuasive, however, because expression of recombinant hTSHR was successful in several mammalian systems (see Stiens et al, Mullins et al, and Takeo et al). Lack of success in bacteria, yeast, and insect cells is not indicative of a lack of success in a transgenic plant system, given that production of the recombinant protein was successful in three different mammalian expression systems. The Applicant has not provided any reports of unsuccessful attempts at expressing hTSHR in any type of plant. There is no teaching or suggestion in the prior art that a plant expression system was not successful for producing hTSHR,

and Whitelam clearly teaches that plant expression systems have proven to be quite successful for producing human therapeutic proteins, such as HSA (see pages 2-5). Therefore, one of ordinary skill in the art would have expected to succeed in expressing recombinant hTSHR in a transgenic plant.

The Applicant further argues that Stiens et al, Mullins et al, and Takeo et al teach away from the use of a plant-based system because they each report the use of mammalian cells (see second paragraph on page 8 of the response).

This is not persuasive, however, because none of these three references teaches that plants would not be a good expression system for hTSHR.

The Applicant further argues that Whitelam's report on the production of recombinant proteins in plants would not motivate one of ordinary skill in the art to attempt to express every animal protein in any plant-based system, which is an improper obvious to try standard (see second paragraph on page 8 of the response).

This is not persuasive, however, because Whitelam's report does suggest that plant expression systems are useful for any valuable protein for pharmaceutical or industrial use (see entire article). The teachings of Stiens et al, Mullins et al, and Takeo et al, would motivate one of ordinary skill in the art to specifically choose hTSHR, because they indicate that recombinant hTSHR would be valuable in diagnostic tests. Even if one applies an obvious to try standard to this combination of references, this is a proper rejection under 35 USC 103, because Stiens et al,

Mullins et al, and Takeo et al clearly teach that there was a recognized need for a good source of recombinant hTSHR in the prior art, and the plant expression systems taught by Whitelam are one of a finite number of expression systems available for production of recombinant proteins, and given the successes of Stiens et al, Mullins et al, and Takeo et al in producing recombinant hTSHR and the successes in producing several recombinant human proteins taught by Whitelam (see pages 2-5), one would have had a reasonable expectation of success in combining the references.

The Applicant argues that the high antigen affinity of the hTSHR produced in their invention is an unexpected result given the problems associated with the use of non-mammalian systems (see paragraph bridging pages 8-9 of the response).

This is not persuasive, however, because the low-affinity results were with proteins that were produced in non-plant systems, and therefore, they are not indicative of what would be expected from the production of hTSHR in a plant.

The Applicant further argues that the instant invention is distinguished over Whitelam because Whitelam reports the need for oleosin as a carrier to improve yields from recombinant expression in plants (see second paragraph on page 9 of the response).

This is not persuasive, however, because the instant claims use "comprise" language that does not exclude the use of an oleosin-hTSHR fusion protein.

Furthermore, while Whitelam teaches that oleosin fusions are a convenient technique for easy purification in plant systems (see right column on page 2), they do not teach that this is a requirement for production of recombinant proteins in plants (see pages 3-5).

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CKW/

/Anne R. Kubelik/
Primary Examiner, Art Unit 1638